REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claims 1-15 have been cancelled without prejudice and replaced with new claims 16-36. New claims 16-28 correspond to former claims 1-14, respectively. The subject matter of claim 15 has been inserted into new claim 16. New claims 29-36 correspond to claims 17-21 and 25-27, respectively, but directed to the test kit. In addition, the new claims have been carefully reworded to include the helpful suggestions proposed by the Examiner, with the exception of the Examiner's suggestion to change the term "determining" in former claim 1 to the term "measuring". This suggestion has not been incorporated into claim 16 for the following reason.

In some embodiments of the invention (see Examples 2 to 4 of the application), there is indeed a measurement of a physical property at the last stage. For instance, in Example 2, the absorbance of a residual solution is measured at a wavelength of 482nm.

However, in other embodiments of the invention, there is only a comparison of the intensity of a signal with a reference (see particularly Example 1). The Applicants believe that the term "measurement" would not be accurate to cover such embodiments.

Thus, the word "determining" is deemed to be more appropriate than "measuring". Please also note that the same word "determining" is used in Claim 1 of U.S. Patent No. 5,434,053 granted by the U.S. Patent Office to Piasio in 1995. Reconsideration is thus requested.

In view of the wording of the new claims, it is believed that the rejection of former claims 1-12 under 35 USC 112, second paragraph, has been overcome as applied to the wording of the new claims.

Lastly, claims 1-12 and 14-15 were rejected under 35 USC 103 as being unpatentable over Piasio in view of either Joris et al. or Zhu et al. This ground of rejection is respectfully traversed.

Piasio (US 5,434,053) describes "a process for the detection of antibiotics in a liquid medium such as milk, urine and blood" (see abstract).

This is obtained with the help of a "labelled antibiotic protein (which) comprises any antibiotic binding protein for example those which may be obtained from an antibiotic-sensitive

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micro-organism, such as a *Bacillus stearothermophilus, Bacillus subtilis, Streptococcus thermophilus* or *Escherichia coli*, preferably *Bacillus stearothermophilus*... (or) antibiotic binding proteins such as antibodies... obtained by immunisation of animals" (see column 2, lines 32-41).

This document neither describes nor suggests use of a recognition agent obtained from *Bacillus lichenformis*. The Examiner correctly acknowledges (page 7 of the Office Action) that "Piasio differs from instant invention in that it does not explicitly disclose the use of BlaR or BlaR-CTD, or any protein obtained from *Bacillus lichenformis*".

The article of Joris et al. (FEMS Microbiology Letters, Vol. 70, 1990, pp. 107-114) reports a university study of "the carboxy terminal domain of the BLAR sensory-transducer protein of *Bacillus lichenformis* as ... penicillin-binding protein" (see title).

There is nothing in this scientific article about detection of antibiotics in biological fluid samples.

As the above-mentioned Joris document, Zhu et al. (Journal of Bacteriology, Vol. 172, No. 2, February 1990, pp. 1137-1141) is a scientific article.

The title reads as follows: "Identification of BlaR, the Signal transducer for β-Lactamase Production in *Bacillus lichenformis*, as a Penicillin-Binding Protein...".

There is nothing more relevant disclosed therein than in previously cited Joris article. Zhu et al. is not concerned with detection of antibiotics in fluid samples.

Piasio explains that detection of antibiotics in liquid media such as milk, urine and blood requires a "a simple test designed to detect low levels of antibiotics in (the) liquid media... The time required for the tests should ideally not exceed about 15 minutes" (column 1, lines 42-46). Piasio lists (column 2, lines 32-37) several microorganisms giving a binding protein permitting to detect antibiotics in the fluid sample after a short time of incubation ("1 to 4 minutes" column 2, line 31).

According to Piasio's example 1, benzylpenicillin residues are detected in milk, with an antibiotic binding protein obtained from *Bacillus stearothermophilus* (column 4, line 25). Column 6, lines 44-46 says: "with this method milk samples with antibiotic residues as little as 5 ppb benzyl penicillin can easily be detected with a total incubation time of 8 minutes".

The reading of this example shows that Piasio's objectives of rapidity (short test time) and sensitivity (detection of low levels of antibiotics in the sample) are met with *Bacillus stearothermophilus*. There is thus no teaching in the reference which would motivate a person skilled in the art to search for another microorganism to make the detection test.

On the other hand, Zhu and Joris articles are university studies of the biochemical nature of BlaR and BlaR-CTD protein of *Bacillus lichenformis*. There is no suggestion of a possible use of such microorganism to detect antibiotics in fluid samples, and besides no suggestion of a possible advantage to such use.

It is further noted that numerous proteins binding β-lactam antibiotics are known, but this does not at all mean that they may form a rapid and stable complex antibiotic-binding protein so as to provide an antibiotics-detection test meeting the objectives of rapidity and sensitivity. In the same way, numerous *Bacillus* microorganisms exist, but this does not mean that they all contain receptors which are suitable for detection of antibiotics in biological fluid samples.

Accordingly, one skilled in the art could not have had a reasonable expectation that the antibiotic binding protein of Zhu et al. or Joris et al. could be used successfully as the recognition agent in the Piasio method based upon the teachings of the cited prior art.

According, favorable reconsideration and allowance is respectfully solicited.

Respectfully submitted,

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